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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/422,528	10/21/1999	WOON-LAM Susan LEUNG	P1190R1	5652

7590 05/04/2006

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EXAMINER
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FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/422,528

Applicant(s)

LEUNG ET AL.

Examiner

Christian L. Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 October 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

1. Claims 1-25 are under consideration in this Office Action.
2. The rejection of claims 1-25 under 35 U.S.C. 112, first paragraph, for failing to meet the written description requirement has been withdrawn in view of applicants' amendment dated 02/09/2006.

### *Claim Rejections - 35 U.S.C. § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-7, 9-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. (BIO/TECHNOLOGY Vol 12, November 1994; PTO 1449 dated 03/06/2000) in view of Wetzel et al. (EP 0155189; PTO1449 dated 03/06/2000).

The teachings of the references have been stated in the previous Office Action.

Applicants' arguments filed 02/09/2006 have been fully considered but they are not persuasive. Applicants' position is that there is no motivation to combine the references of Hart et al. and Wetzel et al., the combination of the references would not make obvious the claimed invention, and the rejection based on impermissible hindsight reconstruction of the claimed invention. The examiner respectfully disagrees for reason of record as supplemented below.

The Hart et al. reference serves as a primary reference that teaches a process for large scale production of IGF-I from the periplasm of *E.coli* comprising culturing *E.coli* host cell having a plasmid comprising an inducible promoter and nucleic acid encoding a signal sequence for secretion into the periplasm linked to human IGF-I. The claims as written do not exclude any type of *in situ* solubilization technique and aqueous two-phase extraction.

The reference of Wetzel et al. teaches that a plasmid vector comprising an inducible promoter and nucleic acid encoding a T4 phage lysozyme. It well known in the art that elimination or reduction of contaminating biological materials including proteoglycan and

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polysaccharide components of the bacterial cell is important for the heterologous expression and purification of a desired protein.

Thus, one of ordinary skill in the art at the time the invention was made would be motivated to eliminate or reduce proteoglycan and polysaccharide components of the *E.coli* bacterial cell wall such that the *E.coli* host cell taught by Hart et al. is further transformed with the plasmid vector of Wetzel et al. Elimination or reduction of proteoglycan and polysaccharide components of the *E.coli* bacterial cell wall by action of the expressed lysozyme would enable a simpler purification of IGF-I or of any desired protein.

The art of recombinant heterologous protein expression in bacterial host cells is well developed and widely used in biotechnology for obtaining a desired protein. Thus, one of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success in modifying the process of Hart et al. such that the *E.coli* host cell taught by Hart et al. is further transformed with the plasmid vector of Wetzel et al. and that a desired protein can be produced by this modified process.

The examiner has not relied on the disclosure to reject the claims under 35 U.S.C. 103(a). Instead, the examiner has determined the scope and contents of the prior art, ascertained the differences between the prior art and the claims at issue, and found the claimed invention to have been obvious in light of the combined teachings of the references.

5. Claim 8 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. in view of Wetzel et al. as applied to the claims above, and further in view of Wick et al. (Infect Immun. 1993 Nov;61(11):4848-56; PTO 892).

The teachings of the references have been stated in the previous Office Action.

The examiner respectfully disagrees with applicants arguments filed 02/09/2006 that the additional reference of Wick et al. does not teach the claimed invention. As stated in the previous Office Action the Wick et al. reference teaches the nucleic acid encoding the lamB signal sequence for expression in the periplasm of *E.coli*. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to further modify the modified method of Hart et al. such that the nucleic acid encoding the lamB signal sequence taught by Wick et al. is used so that the human IGF-I can be secreted into the periplasm of the *E.coli* host cell.

6. Claim 25 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. in view of Wetzel et al. as applied to the claims above, and further in view of Balbas et al. (Gene. 1996 Jun 12;172(1):65-9; PTO 892).

The teachings of the references have been stated in the previous Office Action.

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The examiner respectfully disagrees with applicants arguments filed 02/09/2006 that the additional reference of Balbas et al. does not teach the claimed invention. As stated in the previous Office Action the Balbas et al. reference teaches the plasmid pBRINT which is an efficient vector for chromosomal integration of cloned DNA into the lacZ gene of *E. coli*. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to further modify the modified method of Hart et al. such that the nucleic acid encoding the human IGF-I is cloned into the plasmid pBRINT taught by Balbas et al. which in turn is integrated into the *E.coli* chromosome in order to obtain stability of the nucleic acid encoding the human IGF-I and avoidance of undesired plasmid copy number effects

### *Conclusion*

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF



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